

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: David R. Dilley, Dina K. Kadyrzhanova, Zhenyong Wang
and Toni M. Warner

Application No.: 0 / Group No.:

Filed: Examiner:

For: MODIFIED SYNTHETASES TO PRODUCE PENICILLINS AND CEPHALOSPORINS
UNDER THE CONTROL OF BICARBONATE

Box Sequence

Assistant Commissioner for Patents
Washington, D.C. 20231SUBMISSION OF "SEQUENCE LISTING," COMPUTER READABLE COPY,
AND/OR AMENDMENT PERTAINING THERETO
FOR BIOTECHNOLOGY INVENTION CONTAINING NUCLEOTIDE
AND/OR AMINO ACID SEQUENCE

(check and complete this item, if applicable)

- 1.
- ☐
- This replies to the Office Letter dated _____.

NOTE: If these papers are filed before the office letter issues, adequate identification of the original papers should be made, e.g., in addition to the name of the inventor and title of invention, the filing date based on the "Express Mail" procedure, the application number from the return post card or the attorney's docket number added.

- ☐
- A copy of the Office Letter is enclosed.

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10*

(When using Express Mail, the Express Mail label number is mandatory;
Express Mail certification is optional.)

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

- ☒
- deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

37 C.F.R. § 1.8(a)

37 C.F.R. § 1.10*

- ☐
- with sufficient postage as first class mail.

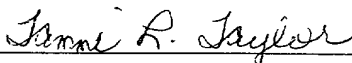
XX as "Express Mail Post Office to Addressee"

Mailing Label No. _____(mandatory)

TRANSMISSION

EJ715841669US

- ☐
- transmitted by facsimile to the Patent and Trademark Office.



Signature

Date: 10/06/99

Tammi L. Taylor

(type or print name of person certifying)

*WARNING: Each paper or fee filed by Express Mail **must** have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. § 1.10(b).

"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will **not** be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.

(Submission—Nucleotide and/or Amino Acid Sequence [9-37]—page 1 of 6)

IDENTIFICATION OF PERSON MAKING STATEMENT

2. I, Ian C. McLeod
(type or print name of declarant signing below)
state the following:

ITEMS BEING SUBMITTED

3. Submitted herewith is/are:
(check each item as applicable)
- A. ☒ "Sequence Listing(s)" for the nucleotide and/or amino acid sequence(s) in this application. Each "Sequence Listing" is assigned a separate identifier as required in 37 C.F.R. § 1.821(c) and 37 C.F.R. §§ 1.822 and 1.823.
 - B. ☐ An amendment to the description and/or claims, wherein reference is made to the sequence by use of the assigned identifier, as required in 37 C.F.R. § 1.821(d).
 - C. ☒ A copy of each "Sequence Listing" submitted for this application in computer readable form, in accordance with the requirements of 37 C.F.R. §§ 1.821(e) and 1.824.
 - D. ☐ Please transfer to this application, in accordance with 37 C.F.R. § 1.821(e), the computer readable copy(ies) from applicant's other application identified as follows:
In re application of:
Application No.: 0 / Group No.:
Filed: Examiner:
For:

The Computer readable form(s) of applicant's other application corresponds to the "Sequence Identifier(s)" of the application as follows:

Computer Readable Form
(other application)

"Sequence Identifier"
(this application)

NOTE: "If the computer readable form of a new application is to be identical with the computer readable form of another application of the applicant on file in the Office, reference may be made to the other application and computer readable form in lieu of filing a duplicate computer readable form in the new application. The new application shall be accompanied by a letter making such reference to the other application and computer readable form, both of which shall be completely identified." 37 C.F.R. § 1.821(e).

- E. ☒ A statement that the content of each "Sequence Listing" submitted and each computer readable copy are the same, as required in 37 C.F.R. § 1.821(g).
- ☐ Because the statement is not made by a person registered to practice before the Office, the statement is verified as required in 37 C.F.R. § 1.821(b).
- F. ☒ Because this submission is made in fulfilling the requirement under 37 C.F.R. § 1.821(g), a statement that the submission includes no new matter.
- ☐ Because the statement is not made by a person registered to practice before the Office, the statement is verified, as required in 37 C.F.R. § 1.821(g).

**STATEMENT THAT "SEQUENCE LISTING"
AND COMPUTER READABLE COPY ARE THE SAME
AND/OR THAT PAPERS SUBMITTED INCLUDES NO NEW MATTER**

4. I hereby state:

(complete applicable item A and/or B)

- A. ☒ Each computer readable form submitted in this application, including those forms requested to be transferred from applicant's other application, is the same as the "Sequence Listing" to which it is indicated to relate.
- B. ☒ All papers accompanying this submission, or for which a request for transfer from applicants' other application, introduce no new matter.

STATUS

5. Applicant is

- ☒ a small entity. A statement:
- ☒ is attached.
- ☐ was already filed.
- ☐ other than a small entity.

(Submission—Nucleotide and/or Amino Acid Sequence [9-37]—page 3 of 6)

EXTENSION OF TERM

6.

NOTE: "Extension of Time in Patent Cases (Supplement Amendments)—If a timely and complete response has been filed after a Non-Final Office Action, an extension of time is not required to permit filing and/or entry of an additional amendment after expiration of the shortened statutory period.

If a timely response has been filed after a Final Office Action, an extension of time is required to permit filing and/or entry of a Notice of Appeal or filing and/or entry of an additional amendment after expiration of the shortened statutory period unless the timely-filed response placed the application in condition for allowance. Of course, if a Notice of Appeal has been filed within the shortened statutory period, the period has ceased to run." Notice of Dec. 10, 1985 (1061 O.G. 34-35).

NOTE: See 37 C.F.R. § 1.645 for extensions of time in interference proceedings and 37 C.F.R. § 1.550(c) for extensions of time in reexamination proceedings.

7. The proceedings herein are for a patent application and the provisions of 37 C.F.R. § 1.136 apply.

(complete (a) or (b) as applicable)

(a) ☐ Applicant petitions for an extension of time under 37 C.F.R. § 1.136 (fees: 37 C.F.R. § 1.17(a)(1)-(4)) for the total number of months checked below:

Extension (months)	Fee for other than small entity	Fee for small entity
<input type="checkbox"/> one month	\$ 110.00	\$ 55.00
<input type="checkbox"/> two months	\$ 380.00	\$ 190.00
<input type="checkbox"/> three months	\$ 870.00	\$ 435.00
<input type="checkbox"/> four months	\$ 1,360.00	\$ 680.00

Fee: \$ _____

If an additional extension of time is required, please consider this a petition therefor.

(check and complete the next item, if applicable)

☐ An extension for _____ months has already been secured. The fee paid therefor of \$_____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request \$_____

OR

(b) ☒ Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition for extension of time.

FEE PAYMENT

8. ☐ Attached is a check in the sum of \$_____.

☐ Charge Account No. _____ the sum of \$_____.

A duplicate of this transmittal is attached.

FEE DEFICIENCY

9.

NOTE: If there is a fee deficiency and there is no authorization to charge an account, additional fees are necessary to cover the additional time consumed in making up the original deficiency. If the maximum, six-month period has expired before the deficiency is noted and corrected, the application is held abandoned. In those instances where authorization to charge is included, processing delays are encountered in returning the papers to the PTO Finance Branch in order to apply these charges prior to action on the cases. Authorization to charge the deposit account for any fee deficiency should be checked. See the Notice of April 7, 1986, 1065 O.G. 31-33.

10. ☒ If any additional extension and/or fee is required, charge

Account No. 13-0610

SIGNATURE(s)

Ian C. McLeod

(type or print name of person signing statement)

10/5/99

Date

Ian C. McLeod

Signature

2190 Commons Parkway

P.O. Address of Signatory

Okemos, Michigan 48864

(if applicable)

Telephone No. (517) 347-4100

Reg. No. 20,931

Customer No.: 21036

- ☐ Inventor(s)
- ☐ Assignee of complete interest
- ☐ Person authorized to sign on behalf of assignee
- ☒ Practitioner of record
- ☐ Filed under Rule 34(a)
- ☐ Registration No. _____
- ☐ Other _____

(specify identity of declarant)

(complete the following, if applicable)

(type name of assignee)

Address of assignee

Title of person authorized to sign on behalf of assignee

A "STATEMENT UNDER 37 C.F.R. § 3.73(b)" is attached.

Reel _____ Frame _____

SIGNATURE OF PRACTITIONER

(type or print name of practitioner)

P.O. Address

Customer No.:

SEQUENCE LISTING

<110> Dilley, David R
Kadyrzhanova, Dina K
Wang, Zhenyong
Warner, Toni M

<120> Modified Synthetases To Produce Penicillins and
Cephalosporins Under the Control of Bicarbonate

<130> MSU 41-453

<140>

<141>

<160> 18

<170> PatentIn Ver. 2.0

<210> 1

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Emericella nidulans strain b1A1

<220>

<221> MUTAGEN

<222> (212)

<223> Glu212 in native IPNS modified to Arg

<400> 1

Met Gly Ser Val Ser Lys Ala Asn Val Pro Lys Ile Asp Val Ser Pro
1 5 10 15

Leu Phe Gly Asp Asp Gln Ala Ala Lys Met Arg Val Ala Gln Gln Ile
20 25 30

Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn His Gly
35 40 45

Ile Asn Val Gln Arg Leu Ser Gln Lys Thr Lys Glu Phe His Met Ser
50 55 60

Ile Thr Pro Glu Glu Lys Trp Asp Leu Ala Ile Arg Ala Tyr Asn Lys
65 70 75 80

Glu His Gln Asp Gln Val Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Gly
85 90 95

Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Thr Pro
100 105 110

Asp His Pro Arg Ile Gln Ala Lys Thr Pro Thr His Glu Val Asn Val
115 120 125

Trp Pro Asp Glu Thr Lys His Pro Gly Phe Gln Asp Phe Ala Glu Gln
130 135 140

Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Lys Gly Tyr
145 150 155 160

Ala Leu Ala Leu Gly Lys Glu Glu Asn Phe Phe Ala Arg His Phe Lys
165 170 175

Pro Asp Asp Thr Leu Ala Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu
180 185 190

Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Ala Ala Asp Gly Thr Lys
195 200 205

Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr
210 215 220

Gln Ser Asn Val Gln Asn Leu Gln Val Glu Thr Ala Ala Gly Tyr Gln
225 230 235 240

Asp Ile Glu Ala Asp Asp Thr Gly Tyr Leu Ile Asn Cys Gly Ser Tyr
245 250 255

Met Ala His Leu Thr Asn Asn Tyr Tyr Lys Ala Pro Ile His Arg Val
260 265 270

Lys Trp Val Asn Ala Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu
275 280 285

Gly Tyr Asp Ser Val Ile Asp Pro Phe Asp Pro Arg Glu Pro Asn Gly
290 295 300

Lys Ser Asp Arg Glu Pro Leu Ser Tyr Gly Asp Tyr Leu Gln Asn Gly
305 310 315 320

Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr
325 330

<210> 2
<211> 331
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: modified IPNS
from Emericella nidulans strain FGSC-4

<220>
<221> MUTAGEN
<222> (212)
<223> Glu212 in native IPNS modified to Arg

<400> 2
Met Gly Ser Val Ser Lys Ala Asn Val Pro Lys Ile Asp Val Ser Pro
1 5 10 15
Leu Phe Gly Asp Asp Gln Ala Ala Lys Met Arg Val Ala Gln Gln Ile
20 25 30
Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn His Gly
35 40 45
Ile Asn Val Gln Arg Leu Ser Gln Lys Thr Lys Glu Phe His Met Ser
50 55 60
Ile Thr Pro Glu Glu Lys Trp Asp Leu Ala Ile Arg Ala Tyr Asn Lys
65 70 75 80
Glu His Gln Asp Gln Val Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Gly
85 90 95
Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Thr Pro
100 105 110
Asp His Pro Arg Ile Gln Ala Lys Thr Pro Thr His Glu Val Asn Val
115 120 125
Trp Pro Asp Glu Thr Lys His Pro Gly Phe Gln Asp Phe Ala Glu Gln
130 135 140
Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Lys Gly Tyr
145 150 155 160
Ala Leu Ala Leu Gly Lys Glu Glu Asn Phe Phe Ala Arg His Phe Lys

165	170	175
Pro Asp Asp Thr Leu Ala Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu		
180	185	190
Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Ala Ala Asp Gly Thr Lys		
195	200	205
Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr		
210	215	220
Gln Ser Asn Val Gln Asn Leu Gln Val Glu Thr Ala Ala Gly Tyr Gln		
225	230	235
Asp Ile Glu Ala Asp Asp Thr Gly Tyr Leu Ile Asn Cys Gly Ser Tyr		
245	250	255
Met Ala His Leu Thr Asn Asn Tyr Tyr Lys Ala Pro Ile His Arg Val		
260	265	270
Lys Trp Val Asn Ala Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu		
275	280	285
Gly Tyr Asp Ser Val Ile Asp Pro Phe Asp Pro Arg Glu Pro Asn Gly		
290	295	300
Lys Ser Asp Arg Glu Pro Leu Ser Tyr Gly Asp Tyr Leu Gln Asn Gly		
305	310	315
Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr		
325	330	

<210> 3

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Emericella nidulans strain bioA1

<220>

<221> MUTAGEN

<222> (212)

<223> Glu212 in native IPNS modified to Arg

<400> 3

Met	Gly	Ser	Val	Ser	Lys	Ala	Asn	Val	Pro	Lys	Ile	Asp	Val	Ser	Pro	1	5	10	15
Leu	Phe	Gly	Asp	Asp	Gln	Ala	Ala	Lys	Met	Arg	Val	Ala	Gln	Gln	Ile	20	25	30	
Asp	Ala	Ala	Ser	Arg	Asp	Thr	Gly	Phe	Phe	Tyr	Ala	Val	Asn	His	Gly	35	40	45	
Ile	Asn	Val	Gln	Arg	Leu	Ser	Gln	Lys	Thr	Lys	Glu	Phe	His	Met	Ser	50	55	60	
Ile	Thr	Pro	Glu	Glu	Lys	Trp	Asp	Leu	Ala	Ile	Arg	Ala	Tyr	Asn	Lys	65	70	75	80
Glu	His	Gln	Asp	Gln	Val	Arg	Ala	Gly	Tyr	Tyr	Leu	Ser	Ile	Pro	Gly	85	90	95	
Lys	Lys	Ala	Val	Glu	Ser	Phe	Cys	Tyr	Leu	Asn	Pro	Asn	Phe	Thr	Pro	100	105	110	
Asp	His	Pro	Arg	Ile	Gln	Ala	Lys	Thr	Pro	Thr	His	Glu	Val	Asn	Val	115	120	125	
Trp	Pro	Asp	Glu	Thr	Lys	His	Pro	Gly	Phe	Gln	Asp	Phe	Ala	Glu	Gln	130	135	140	
Tyr	Tyr	Trp	Asp	Val	Phe	Gly	Leu	Ser	Ser	Ala	Leu	Leu	Lys	Gly	Tyr	145	150	155	160
Ala	Leu	Ala	Leu	Gly	Lys	Glu	Glu	Asn	Phe	Phe	Ala	Arg	His	Phe	Lys	165	170	175	
Pro	Asp	Asp	Thr	Leu	Ala	Ser	Val	Val	Leu	Ile	Arg	Tyr	Pro	Tyr	Leu	180	185	190	
Asp	Pro	Tyr	Pro	Glu	Ala	Ala	Ile	Lys	Thr	Ala	Ala	Asp	Gly	Thr	Lys	195	200	205	
Leu	Ser	Phe	Arg	Trp	His	Glu	Asp	Val	Ser	Leu	Ile	Thr	Val	Leu	Tyr	210	215	220	
Gln	Ser	Asn	Val	Gln	Asn	Leu	Gln	Val	Glu	Thr	Ala	Ala	Gly	Tyr	Gln	225	230	235	240
Asp	Ile	Glu	Ala	Asp	Asp	Thr	Gly	Tyr	Leu	Ile	Asn	Cys	Gly	Ser	Tyr	245	250	255	

Met Ala His Leu Thr Asn Asn Tyr Tyr Lys Ala Pro Ile His Arg Val
 260 265 270

Lys Trp Val Asn Ala Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu
 275 280 285

Gly Tyr Asp Ser Val Ile Asp Pro Phe Asp Pro Arg Glu Pro Asn Gly
 290 295 300

Lys Ser Asp Arg Glu Pro Leu Ser Tyr Gly Asp Tyr Leu Gln Asn Gly
 305 310 315 320

Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr
 325 330

<210> 4

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
 from Penicillium chrysogenum

<220>

<221> MUTAGEN

<222> (212)

<223> Glu212 in native IPNS modified to Arg

<400> 4

Met Ala Ser Thr Pro Lys Ala Asn Val Pro Lys Ile Asp Val Ser Pro
 1 5 10 15

Leu Phe Gly Asp Asn Met Glu Glu Lys Met Lys Val Ala Arg Ala Ile
 20 25 30

Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn His Gly
 35 40 45

Val Asp Val Lys Arg Leu Ser Asn Lys Thr Arg Glu Phe His Phe Ser
 50 55 60

Ile Thr Asp Glu Glu Lys Trp Asp Leu Ala Ile Arg Ala Tyr Asn Lys
 65 70 75 80

Glu His Gln Asp Gln Ile Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Glu
 85 90 95

Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Lys Pro
 100 105 110

Asp His Pro Leu Ile Gln Ser Lys Thr Pro Thr His Glu Val Asn Val
 115 120 125

Trp Pro Asp Glu Lys Lys His Pro Gly Phe Arg Glu Phe Ala Glu Gln
 130 135 140

Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Arg Gly Tyr
 145 150 155 160

Ala Leu Ala Leu Gly Lys Glu Glu Asp Phe Phe Ser Arg His Phe Lys
 165 170 175

Lys Glu Asp Ala Leu Ser Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu
 180 185 190

Asn Pro Ile Pro Pro Ala Ala Ile Lys Thr Ala Glu Asp Gly Thr Lys
 195 200 205

Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr
 210 215 220

Gln Ser Asp Val Ala Asn Leu Gln Val Glu Met Pro Gln Gly Tyr Leu
 225 230 235 240

Asp Ile Glu Ala Asp Asp Asn Ala Tyr Leu Val Asn Cys Gly Ser Tyr
 245 250 255

Met Ala His Ile Thr Asn Asn Tyr Tyr Pro Ala Pro Ile His Arg Val
 260 265 270

Lys Trp Val Asn Glu Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu
 275 280 285

Gly Phe Asn Asp Thr Val Gln Pro Trp Asp Pro Ser Lys Glu Asp Gly
 290 295 300

Lys Thr Asp Gln Arg Pro Ile Ser Tyr Gly Asp Tyr Leu Gln Asn Gly
 305 310 315 320

Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr
 325 330

<210> 5

<211> 329
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Streptomyces clavuligerus

<220>

<221> MUTAGEN

<222> (210)

<223> Glu210 in native IPNS modified to Arg

<400> 5

Met Pro Val Leu Met Pro Ser Ala His Val Pro Thr Ile Asp Ile Ser
1 5 10 15

Pro Leu Phe Gly Thr Asp Ala Ala Ala Lys Lys Arg Val Ala Glu Glu
20 25 30

Ile His Gly Ala Cys Arg Gly Ser Gly Phe Phe Tyr Ala Thr Asn His
35 40 45

Gly Val Asp Val Gln Gln Leu Gln Asp Val Val Asn Glu Phe His Gly
50 55 60

Ala Met Thr Asp Gln Glu Lys His Asp Leu Ala Ile His Ala Tyr Asn
65 70 75 80

Pro Asp Asn Pro His Val Arg Asn Gly Tyr Tyr Lys Ala Val Pro Gly
85 90 95

Arg Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asp Phe Gly Glu
100 105 110

Asp His Pro Met Ile Ala Ala Gly Thr Pro Met His Glu Val Asn Leu
115 120 125

Trp Pro Asp Glu Glu Arg His Pro Arg Phe Arg Pro Phe Cys Glu Gly
130 135 140

Tyr Tyr Arg Gln Met Leu Lys Leu Ser Thr Val Leu Met Arg Gly Leu
145 150 155 160

Ala Leu Ala Leu Gly Arg Pro Glu His Phe Phe Asp Ala Ala Leu Ala
165 170 175

Glu Gln Asp Ser Leu Ser Ser Val Ser Leu Ile Arg Tyr Pro Tyr Leu

180	185	190
Glu Glu Tyr Pro Pro Val Lys Thr Gly Pro Asp Gly Gln Leu Leu Ser		
195	200	205
Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val Leu Phe Gln Thr		
210	215	220
Gln Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly Trp Arg Asp Ile		
225	230	240
Pro Thr Ser Glu Asn Asp Phe Leu Val Asn Cys Gly Thr Tyr Met Ala		
245	250	255
His Val Thr Asn Asp Tyr Phe Pro Ala Pro Asn His Arg Val Lys Phe		
260	265	270
Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu Asn Gly Gly His		
275	280	285
Glu Ala Val Ile Glu Pro Phe Val Pro Glu Gly Ala Ser Glu Glu Val		
290	295	300
Arg Asn Glu Ala Leu Ser Tyr Gly Asp Tyr Leu Gln His Gly Leu Arg		
305	310	315
Ala Leu Ile Val Lys Asn Gly Gln Thr		
325		

<210> 6

<211> 338

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Acremonium chrysogenum

<220>

<221> MUTAGEN

<222> (214)

<223> Glu214 in native IPNS modified to Arg

<400> 6

Met Gly Ser Val Pro Val Pro Val Ala Asn Val Pro Arg Ile Asp Val
1 5 10 15

Ser	Pro	Leu	Phe	Gly	Asp	Asp	Lys	Glu	Lys	Lys	Leu	Glu	Val	Ala	Arg	20	25	30
Ala	Ile	Asp	Ala	Ala	Ser	Arg	Asp	Thr	Gly	Phe	Phe	Tyr	Ala	Val	Asn	35	40	45
His	Gly	Val	Asp	Leu	Pro	Trp	Leu	Ser	Arg	Glu	Thr	Asn	Lys	Phe	His	50	55	60
Met	Ser	Ile	Thr	Asp	Glu	Glu	Lys	Trp	Gln	Leu	Ala	Ile	Arg	Ala	Tyr	65	70	75
Asn	Lys	Glu	His	Glu	Ser	Gln	Ile	Arg	Ala	Gly	Tyr	Tyr	Leu	Pro	Ile	85	90	95
Pro	Gly	Lys	Lys	Ala	Val	Glu	Ser	Phe	Cys	Tyr	Leu	Asn	Pro	Ser	Phe	100	105	110
Ser	Pro	Asp	His	Pro	Arg	Ile	Lys	Glu	Pro	Thr	Pro	Met	His	Glu	Val	115	120	125
Asn	Val	Trp	Pro	Asp	Glu	Ala	Lys	His	Pro	Gly	Phe	Arg	Ala	Phe	Ala	130	135	140
Glu	Lys	Tyr	Tyr	Trp	Asp	Val	Phe	Gly	Leu	Ser	Ser	Ala	Val	Leu	Arg	145	150	155
Gly	Tyr	Ala	Leu	Ala	Leu	Gly	Arg	Asp	Glu	Asp	Phe	Phe	Thr	Arg	His	165	170	175
Ser	Arg	Arg	Asp	Thr	Thr	Leu	Ser	Ser	Val	Val	Leu	Ile	Arg	Tyr	Pro	180	185	190
Tyr	Leu	Asp	Pro	Tyr	Pro	Glu	Pro	Ala	Ile	Lys	Thr	Ala	Asp	Asp	Gly	195	200	205
Thr	Lys	Leu	Ser	Phe	Arg	Trp	His	Glu	Asp	Val	Ser	Leu	Ile	Thr	Val	210	215	220
Leu	Tyr	Gln	Ser	Asp	Val	Gln	Asn	Leu	Gln	Val	Lys	Thr	Pro	Gln	Gly	225	230	235
Trp	Gln	Asp	Ile	Gln	Ala	Asp	Asp	Thr	Gly	Phe	Leu	Ile	Asn	Cys	Gly	245	250	255
Ser	Tyr	Met	Ala	His	Ile	Thr	Asp	Asp	Tyr	Tyr	Pro	Ala	Pro	Ile	His	260	265	270

Arg Val Lys Trp Val Asn Glu Glu Arg Gln Ser Leu Pro Phe Phe Val
 275 280 285

Asn Leu Gly Trp Glu Asp Thr Ile Gln Pro Trp Asp Pro Ala Thr Ala
 290 295 300

Lys Asp Gly Ala Lys Asp Ala Ala Lys Asp Lys Pro Ala Ile Ser Tyr
 305 310 315 320

Gly Glu Tyr Leu Gln Gly Gly Leu Arg Gly Leu Ile Asn Lys Asn Gly
 325 330 335

Gln Thr

<210> 7

<211> 338

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
 from Acremonium chrysogenum strain M8650

<220>

<221> MUTAGEN

<222> (214)

<223> Glu214 in native IPNS modified to Arg

<400> 7

Met Gly Ser Val Pro Val Pro Val Ala Asn Val Pro Arg Ile Asp Val
 1 5 10 15

Ser Pro Leu Phe Gly Asp Asp Lys Glu Lys Lys Leu Glu Val Ala Arg
 20 25 30

Ala Ile Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn
 35 40 45

His Gly Val Asp Leu Pro Trp Leu Ser Arg Glu Thr Asn Lys Phe His
 50 55 60

Met Ser Ile Thr Asp Glu Glu Lys Trp Gln Leu Ala Ile Arg Ala Tyr
 65 70 75 80

Asn Lys Glu His Glu Ser Gln Ile Arg Ala Gly Tyr Tyr Leu Pro Ile
 85 90 95

Pro Gly Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Ser Phe
 100 105 110

Ser Pro Asp His Pro Arg Ile Lys Glu Pro Thr Pro Met His Glu Val
 115 120 125

Asn Val Trp Pro Asp Glu Ala Lys His Pro Gly Phe Arg Ala Phe Ala
 130 135 140

Glu Lys Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Val Leu Arg
 145 150 155 160

Gly Tyr Ala Leu Ala Leu Gly Arg Asp Glu Asp Phe Phe Thr Arg His
 165 170 175

Phe Arg Arg Asp Thr Thr Leu Ser Ser Val Val Leu Ile Arg Tyr Pro
 180 185 190

Tyr Leu Asp Pro Tyr Pro Glu Pro Ala Ile Lys Thr Ala Asp Asp Gly
 195 200 205

Thr Lys Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val
 210 215 220

Leu Tyr Gln Ser Asp Val Gln Asn Leu Gln Val Lys Thr Pro Gln Gly
 225 230 235 240

Trp Gln Asp Ile Gln Ala Asp Asp Thr Gly Phe Leu Ile Asn Cys Gly
 245 250 255

Ser Tyr Met Ala His Ile Thr Asp Asp Tyr Tyr Pro Ala Pro Ile His
 260 265 270

Arg Val Lys Trp Val Asn Glu Glu Arg Gln Ser Leu Pro Phe Phe Val
 275 280 285

Asn Leu Gly Trp Glu Asp Thr Ile Gln Pro Trp Asp Pro Ala Thr Ala
 290 295 300

Lys Asp Gly Ala Lys Asp Ala Ala Lys Asp Lys Pro Ala Ile Ser Tyr
 305 310 315 320

Gly Glu Tyr Leu Gln Gly Gly Leu Arg Gly Leu Ile Asn Lys Asn Gly
 325 330 335

Gln Thr

<210> 8
 <211> 321
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: modified IPNS
 from Streptomyces cattleya

<220>
 <221> MUTAGEN
 <222> (211)
 <223> Glu211 in native IPNS modified to Arg

<400> 8
 Met Pro Val Leu Met Pro Ser Ala Asp Val Pro Thr Ile Asp Ile Ser
 1 5 10 15

Pro Gln Leu Phe Gly Thr Asp Pro Thr Pro Arg Arg Thr Ser Arg Gly
 20 25 30

Arg Ser Thr Arg Pro Ala Arg Gly Ser Gly Phe Phe Tyr Ala Ser His
 35 40 45

His Gly Ile Asp Val Arg Arg Leu Gln Thr Trp Ser Asn Glu Ser Thr
 50 55 60

Thr Met Thr Asp Gln Arg Ser Thr Thr Trp Arg Ser Thr Arg Tyr Asn
 65 70 75 80

Glu Asn Asn Ser His Val Arg Asn Gly Tyr Tyr Met Ala Arg Pro Gly
 85 90 95

Arg Glu Thr Val Glu Ser Trp Cys Tyr Leu Asn Pro Ser Phe Gly Glu
 100 105 110

Asp His Pro Met Met Lys Ala Gly Thr Pro Met His Glu Val Asn Val
 115 120 125

Trp Pro Asp Glu Glu Arg His Pro Asp Phe Gly Ser Phe Gly Glu Gln
 130 135 140

Tyr His Arg Glu Val Ser Ala Ser Arg Arg Cys Cys Cys Gly Ala Ser
 145 150 155 160

Arg Trp Arg Arg Gln Ala Gly Glu Ser Ser Ser Asn Glu Val Thr Glu

	165		170		175
Glu Asp Thr Leu Ser Ala Val Ser Met Ile Arg Tyr Pro Tyr Leu Asp					
	180		185		190
Pro Tyr Pro Glu Ala Ala Ile Lys Thr Gly Pro Asp Gly Thr Arg Leu					
	195		200		205
Ser Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val Leu Ser Lys					
	210		215		220
Thr Glu Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly Trp Gln Ser					
	225		230		240
Leu Pro Thr Ser Gly Glu Asn Phe Leu Ile Asn Cys Gly Thr Tyr Leu					
		245		250	255
Gly Tyr Leu Thr Asn Asp Tyr Phe Pro Ala Pro Asn His Arg Val Lys					
	260		265		270
Tyr Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu His Ala Gly					
	275		280		285
Gln Asn Ser Val Met Lys Pro Phe Thr Arg Arg Thr Gly Asp Arg Lys					
	290		295		300
Leu Asn Pro Ala Val Thr Tyr Gly Glu Tyr Leu Gln Glu Gly Phe Thr					
	305		310		315
					320

Arg

<210> 9

<211> 329

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Streptomyces clavuligerus strain NRRL 3585

<220>

<221> MUTAGEN

<222> (210)

<223> Glu210 in native IPNS modified to Arg

<400> 9

Met	Pro	Val	Leu	Met	Pro	Ser	Ala	His	Val	Pro	Thr	Ile	Asp	Ile	Ser	1	5	10	15
Pro	Leu	Phe	Gly	Thr	Asp	Ala	Ala	Ala	Lys	Lys	Arg	Val	Ala	Glu	Glu	20	25	30	
Ile	His	Gly	Ala	Cys	Arg	Gly	Ser	Gly	Phe	Phe	Tyr	Ala	Thr	Asn	His	35	40	45	
Gly	Val	Asp	Val	Gln	Gln	Leu	Gln	Asp	Val	Val	Asn	Glu	Phe	His	Gly	50	55	60	
Ala	Met	Thr	Asp	Gln	Glu	Lys	His	Asp	Leu	Ala	Ile	His	Ala	Tyr	Asn	65	70	75	80
Pro	Asp	Asn	Pro	His	Val	Arg	Asn	Gly	Tyr	Tyr	Lys	Ala	Val	Pro	Gly	85	90	95	
Arg	Lys	Ala	Val	Glu	Ser	Phe	Cys	Tyr	Leu	Asn	Pro	Asp	Phe	Gly	Glu	100	105	110	
Asp	His	Pro	Met	Ile	Ala	Ala	Gly	Thr	Pro	Met	His	Glu	Val	Asn	Leu	115	120	125	
Trp	Pro	Asp	Glu	Glu	Arg	His	Pro	Arg	Phe	Arg	Pro	Phe	Cys	Glu	Gly	130	135	140	
Tyr	Tyr	Arg	Gln	Met	Leu	Lys	Leu	Ser	Thr	Val	Leu	Met	Arg	Gly	Leu	145	150	155	160
Ala	Leu	Ala	Leu	Gly	Arg	Pro	Glu	His	Phe	Phe	Asp	Ala	Ala	Leu	Ala	165	170	175	
Glu	Gln	Asp	Ser	Leu	Ser	Ser	Val	Ser	Leu	Ile	Arg	Tyr	Pro	Tyr	Leu	180	185	190	
Glu	Glu	Tyr	Pro	Pro	Val	Lys	Thr	Gly	Pro	Asp	Gly	Gln	Leu	Leu	Ser	195	200	205	
Phe	Arg	Asp	His	Leu	Asp	Val	Ser	Met	Ile	Thr	Val	Leu	Phe	Gln	Thr	210	215	220	
Gln	Val	Gln	Asn	Leu	Gln	Val	Glu	Thr	Val	Asp	Gly	Trp	Arg	Asp	Ile	225	230	235	240
Pro	Thr	Ser	Glu	Asn	Asp	Phe	Leu	Val	Asn	Cys	Gly	Thr	Tyr	Met	Ala	245	250	255	

His Val Thr Asn Asp Tyr Phe Pro Ala Pro Asn His Arg Val Lys Phe
260 265 270

Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu Asn Gly Gly His
275 280 285

Glu Ala Val Ile Glu Pro Phe Val Pro Glu Gly Ala Ser Glu Glu Val
290 295 300

Arg Asn Glu Ala Leu Ser Tyr Gly Asp Tyr Leu Gln His Gly Leu Arg
305 310 315 320

Ala Leu Ile Val Lys Asn Gly Gln Thr
325

<210> 10

<211> 333

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from streptomyces anulatus (S. lipmanii)

<220>

<221> MUTAGEN

<222> (214)

<223> Glu214 in native IPNS modified to Arg

<400> 10

Met Pro Val Leu Met Pro Ser Ala Asp Val Pro Thr Ile Asp Ile Ser
1 5 10 15

Pro Leu Phe Gly Thr Asp Pro Asp Ala Lys Ala His Val Ala Arg Gln
20 25 30

Ile Asn Glu Ala Cys Arg Gly Ser Gly Phe Phe Tyr Ala Ser His His
35 40 45

Gly Ile Asp Val Arg Arg Leu Gln Asp Val Val Asn Glu Phe His Arg
50 55 60

Thr Met Thr Asp Gln Glu Lys His Asp Leu Ala Ile His Ala Tyr Asn
65 70 75 80

Glu Asn Asn Ser His Val Arg Asn Gly Tyr Tyr Met Ala Arg Pro Gly
85 90 95

Arg Lys Thr Val Glu Ser Trp Cys Tyr Leu Asn Pro Ser Phe Gly Glu
 100 105 110

Asp His Pro Met Ile Lys Ala Gly Thr Pro Met His Glu Val Asn Val
 115 120 125

Trp Pro Asp Glu Glu Arg His Pro Asp Phe Arg Ser Phe Gly Glu Gln
 130 135 140

Tyr Tyr Arg Glu Val Phe Arg Leu Ser Lys Val Leu Leu Leu Arg Gly
 145 150 155 160

Phe Ala Leu Ala Leu Gly Lys Pro Glu Glu Phe Phe Glu Asn Glu Val
 165 170 175

Thr Glu Glu Asp Thr Leu Ser Cys Arg Ser Leu Met Ile Arg Tyr Pro
 180 185 190

Tyr Leu Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Gly Pro Asp Gly
 195 200 205

Thr Arg Leu Ser Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val
 210 215 220

Leu Phe Gln Thr Glu Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly
 225 230 235 240

Trp Gln Ser Leu Pro Thr Ser Gly Glu Asn Phe Leu Ile Asn Cys Gly
 245 250 255

Thr Tyr Leu Gly Tyr Leu Thr Asn Asp Tyr Phe Pro Ala Pro Asn His
 260 265 270

Arg Val Lys Tyr Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu
 275 280 285

His Ala Gly Gln Asn Ser Val Met Lys Pro Phe His Pro Glu Asp Thr
 290 295 300

Gly Asp Arg Lys Leu Asn Pro Ala Val Thr Tyr Gly Glu Tyr Leu Gln
 305 310 315 320

Glu Gly Phe His Ala Leu Ile Ala Lys Asn Val Gln Thr
 325 330

<210> 11

<211> 21
<212> PRT
<213> Emericella nidulans

<220>
<221> PEPTIDE
<222> (1)..(21)
<223> corresponds to amino acids 205 to 225 of native
IPNS

<400> 11
Asp Gly Thr Lys Leu Ser Phe Glu Trp His Glu Asp Val Ser Leu Ile
1 5 10 15

Thr Val Leu Tyr Gln
20

<210> 12
<211> 21
<212> PRT
<213> Penicillium chrysogenum

<220>
<221> PEPTIDE
<222> (1)..(21)
<223> corresponds to amino acids 205 to 225 of native
IPNS

<400> 12
Asp Gly Thr Lys Leu Ser Phe Glu Trp His Glu Asp Val Ser Leu Ile
1 5 10 15

Thr Val Leu Tyr Gln
20

<210> 13
<211> 21
<212> PRT
<213> Acremonium chrysogenum

<220>
<221> PEPTIDE
<222> (1)..(21)
<223> corresponds to amino acids 207 to ss7 of native
IPNS

<400> 13

Asp Gly Thr Lys Leu Ser Phe Glu Trp His Glu Asp Val Ser Leu Ile
1 5 10 15

Thr Val Leu Tyr Gln
20

<210> 14

<211> 21

<212> PRT

<213> Streptomyces clavuligerus

<220>

<221> PEPTIDE

<222> (1)..(21)

<223> corresponds to amino acids 302 to 223 of native
IPNS

<400> 14

Asp Gly Gln Leu Leu Ser Phe Glu Asp His Leu Asp Val Ser Met Ile
1 5 10 15

Thr Val Leu Phe Gln
20

<210> 15

<211> 21

<212> PRT

<213> Streptomyces cattleya

<220>

<221> PEPTIDE

<222> (1)..(21)

<223> corresponds to amino acids 204 to 224 of native
IPNS

<400> 15

Asp Gly Thr Arg Leu Ser Phe Glu Asp His Leu Asp Val Ser Met Ile
1 5 10 15

Thr Val Leu Ser Glu
20

<210> 16

<211> 21

<212> PRT

<213> Streptomyces anulatus

<220>

<221> PEPTIDE

<222> (1)..(21)

<223> corresponds to amino acids 207 to 227 of native
IPNS

<400> 16

Asp Gly Thr Arg Leu Ser Phe Glu Asp His Leu Asp Val Ser Met Ile
1 5 10 15

Thr Val Leu Phe Gln
20

<210> 17

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutagenic
oligonucleotide primer

<400> 17

ctgagttttg agtggcatcg ggatgtaatc 30

<210> 18

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified DAOCS
from Streptomyces clavuligerus

<220>

<221> MUTAGEN

<222> (181)

<223> Ala181 in native DAOCS modified to Arg

<400> 18

Met Asp Thr Thr Val Pro Thr Phe Ser Leu Ala Glu Leu Gln Gln Gly
1 5 10 15

Leu His Gln Asp Glu Phe Arg Arg Cys Leu Arg Asp Lys Gly Leu Phe

20	25	30
Tyr Leu Thr Asp Cys Gly Leu Thr Asp Thr Glu Leu Lys Ser Ala Lys		
35	40	45
Asp Leu Val Ile Asp Phe Phe Glu His Gly Ser Glu Ala Glu Lys Arg		
50	55	60
Ala Val Thr Ser Pro Val Pro Thr Met Arg Arg Gly Phe Thr Gly Leu		
65	70	75
Glu Ser Glu Ser Thr Ala Gln Ile Thr Asn Thr Gly Ser Tyr Ser Asp		
85	90	95
Tyr Ser Met Cys Tyr Ser Met Gly Thr Ala Asp Asn Leu Phe Pro Ser		
100	105	110
Gly Asp Phe Glu Arg Ile Trp Thr Gln Tyr Phe Asp Arg Gln Tyr Thr		
115	120	125
Ala Ser Arg Ala Val Ala Arg Glu Val Leu Arg Ala Thr Gly Thr Glu		
130	135	140
Pro Asp Gly Gly Val Glu Ala Phe Leu Asp Cys Glu Pro Leu Leu Arg		
145	150	155
Phe Arg Tyr Phe Pro Gln Val Pro Glu His Arg Ser Ala Glu Glu Gln		
165	170	175
Pro Leu Arg Met Arg Pro His Tyr Asp Leu Ser Met Val Thr Leu Ile		
180	185	190
Gln Gln Thr Pro Cys Ala Asn Gly Phe Val Ser Leu Gln Ala Glu Val		
195	200	205
Gly Gly Ala Phe Thr Asp Leu Pro Tyr Arg Pro Asp Ala Val Leu Val		
210	215	220
Phe Cys Gly Ala Ile Ala Thr Leu Val Thr Gly Gly Gln Val Lys Ala		
225	230	235
Pro Arg His His Val Ala Ala Pro Arg Arg Asp Gln Ile Ala Gly Ser		
245	250	255
Ser Arg Thr Ser Ser Val Phe Phe Leu Arg Pro Asn Ala Asp Phe Thr		
260	265	270
Phe Ser Val Pro Leu Ala Arg Glu Cys Gly Phe Asp Val Ser Leu Asp		

285

Ile Arg Arg Thr Ser Lys Ala
305 310